

10/625024

=> d his

(FILE 'HOME' ENTERED AT 17:15:18 ON 10 JAN 2005)

FILE 'REGISTRY' ENTERED AT 17:15:50 ON 10 JAN 2005

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L5 STRUCTURE UPLOADED  
L6 0 S L5  
L7 STRUCTURE UPLOADED  
L8 23 S L7  
L9 STRUCTURE UPLOADED  
L10 2 S L9  
L11 STRUCTURE UPLOADED  
L12 5 S L11  
L13 83 S L11 SSS FULL  
L14 79 S L13/COMPLETE

FILE 'CAPLUS' ENTERED AT 18:30:13 ON 10 JAN 2005

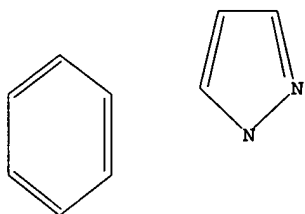
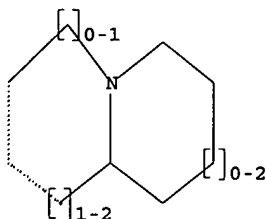
L15 10 S L14

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L11 HAS NO ANSWERS

L11 STR

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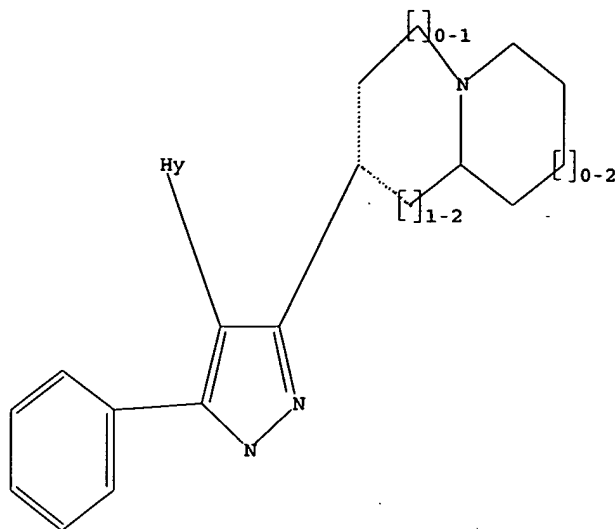


Structure attributes must be viewed using STN Express query preparation.

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L9 HAS NO ANSWERS

L9 STR



Structure attributes must be viewed using STN Express query preparation.

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L5 HAS NO ANSWERS  
L5 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

=> d 1-10 bib abs hitstr

L15 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2004:80689 CAPLUS  
DN 140:146132  
TI Preparation of bicyclic unsaturated tertiary amine compounds as inhibitors  
of production of inflammatory cytokines  
IN Kimura, Tomio; Ohkawa, Nobuyuki; Aoki, Kazumasa; Nakao, Akira; Nagasaki,  
Takayoshi  
PA Sankyo Company, Limited, Japan  
SO PCT Int. Appl., 244 pp.  
CODEN: PIXXD2  
DT Patent  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004009592	A1	20040129	WO 2003-JP9110	20030717
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	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
	CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				
	GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				
	LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,				
	PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,				
	TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				
	KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,				
	FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,				
	BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	JP 2004099600	A2	20040402	JP 2003-199729	20030722
PRAI	JP 2002-211836	A	20020719		
OS	MARPAT 140:146132				
AB	The title compds. R1R2AR3 [wherein A represents pyrrole or pyrazole; R1 represents optionally substituted aryl or heteroaryl; R2 represents optionally substituted heteroaryl; and R3 represents indolizine] are prepared In an in vitro assay using human whole blood, compds. of this invention showed IC50 values of 2.1 nM to 7.8 nM against TNFα release. Formulations are given.				
IT	651736-17-3P 651736-19-5P 651736-21-9P 651736-29-7P 651736-42-4P 651736-43-5P				

10/625024

651736-44-6P 651736-63-9P

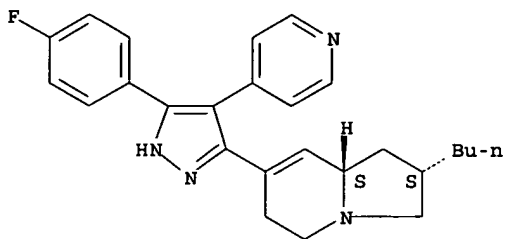
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

(preparation of bicyclic unsatd. tertiary amine compds. as inhibitors of  
production of inflammatory cytokines)

RN 651736-17-3 CAPLUS

CN Indolizine, 2-butyl-7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-  
1,2,3,5,6,8a-hexahydro-, (2S,8aS)- (9CI) (CA INDEX NAME)

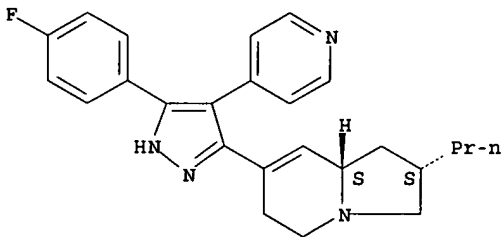
Absolute stereochemistry.



RN 651736-19-5 CAPLUS

CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-  
1,2,3,5,6,8a-hexahydro-2-propyl-, (2S,8aS)- (9CI) (CA INDEX NAME)

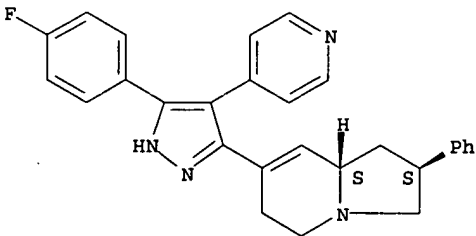
Absolute stereochemistry.



RN 651736-21-9 CAPLUS

CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-  
1,2,3,5,6,8a-hexahydro-2-phenyl-, (2S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

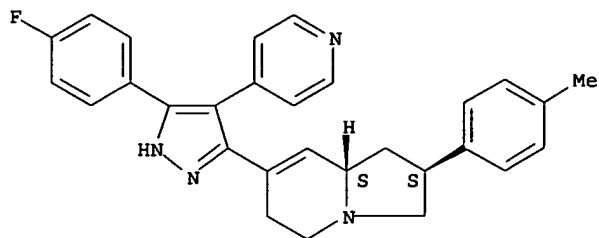


RN 651736-29-7 CAPLUS

CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-  
1,2,3,5,6,8a-hexahydro-2-(4-methylphenyl)-, (2S,8aS)- (9CI) (CA INDEX  
NAME)

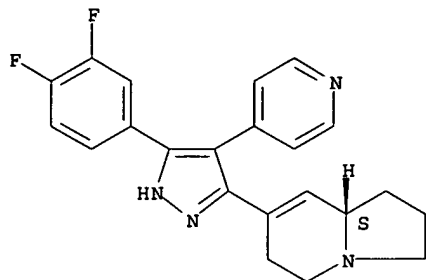
Absolute stereochemistry.

10/625024



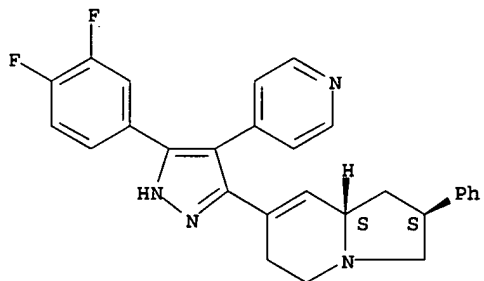
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CN Indolizine, 7-[5-(3,4-difluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro-, (8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



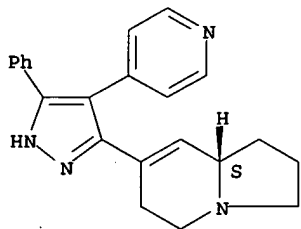
RN 651736-43-5 CAPLUS  
CN Indolizine, 7-[5-(3,4-difluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro-2-phenyl-, (2S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 651736-44-6 CAPLUS  
CN Indolizine, 1,2,3,5,6,8a-hexahydro-7-[5-phenyl-4-(4-pyridinyl)-1H-pyrazol-3-yl]-, (8aS)- (9CI) (CA INDEX NAME)

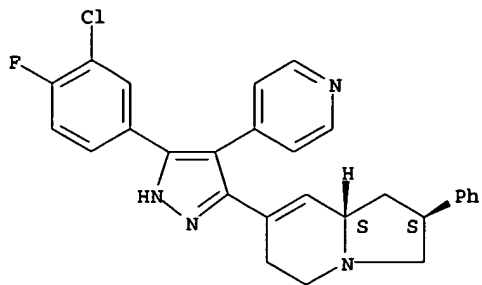
Absolute stereochemistry.



RN 651736-63-9 CAPLUS  
CN Indolizine, 7-[5-(3-chloro-4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro-2-phenyl-, (2S,8aS)- (9CI) (CA INDEX NAME)

10/625024

Absolute stereochemistry.



IT 651736-64-0P

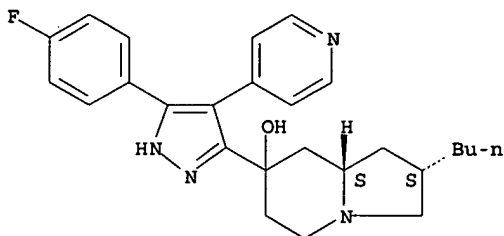
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of bicyclic unsatd. tertiary amine compds. as inhibitors of production of inflammatory cytokines)

RN 651736-64-0 CAPLUS

CN 7-Indolizinol, 2-butyl-7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]octahydro-, (2S,8aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:80686 CAPLUS

DN 140:146157

TI Preparation of pyrazolopyridinylpyrimidines as inhibitors of cGMP degradation for the treatment of central nervous system diseases

IN Feurer, Achim; Luithle, Joachim; Wirtz, Stephan-nicholas; Koenig, Gerhard; Stasch, Johannes-peter; Stahl, Elke; Schreiber, Rudy; Wunder, Frank; Lang, Dieter

PA Bayer Healthcare Ag, Germany

SO PCT Int. Appl., 96 pp.

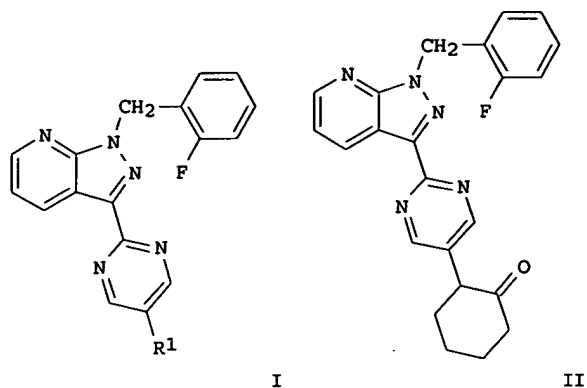
CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

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WO 2004009589	A1	20040129	WO 2003-EP7238	20030707
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10232572	A1	20040205	DE 2002-10232572	20020718
PRAI DE 2002-10232572	A	20020718		
OS MARPAT 140:146157				
GI				

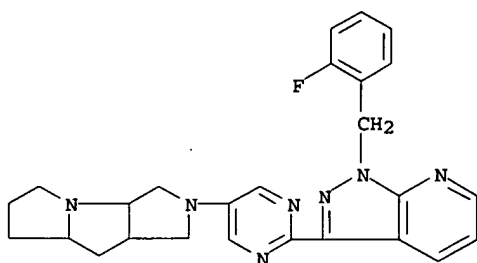


AB Title compds. I [R1 = (un)substituted aryl, heteroaryl, benzodioxole, etc.] and their pharmaceutically acceptable salts were prepared For example, palladium mediated coupling of bromide I [R1 = Br], e.g., prepared from 2-fluorobenzylhydrazine in 6-steps, and cyclohexanone afforded pyrazolopyridinylpyrimidine II in 29% yield. In cGMP degradation inhibition assays, 10-examples of compds. I exhibited a significant increase (sic) in cGMP concentration at 0.27-1.2  $\mu$ M inhibitor concentration Compds. I are claimed useful for the treatment of learning, concentration and perception disorders.

IT 651339-87-6P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (target compound; preparation of pyrazolopyridinylpyrimidines as inhibitors of cGMP degradation for the treatment of central nervous system diseases)

RN 651339-87-6 CAPLUS

CN Pyrrolo[3,4-b]pyrrolizine, 2-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]decahydro- (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2003:154248 CAPLUS  
 DN 138:204948  
 TI Preparation of 4-(1,2,3,5,6,8a-hexahydroindolizin-7-yl)-3-(pyridin-4-yl)-1H-pyrrole derivatives and related compounds and novel antidiabetic pharmaceutical compositions containing them  
 IN Fujiwara, Toshihiko; Ushiyama, Shigeru; Kimura, Tomio  
 PA Sankyo Company, Limited, Japan  
 SO PCT Int. Appl., 473 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003015781	A1	20030227	WO 2002-JP8276	20020814

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

JP 2003128551

A2

20030508

JP 2002-234617

20020812

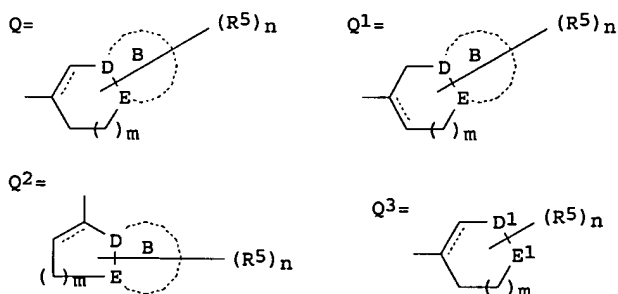
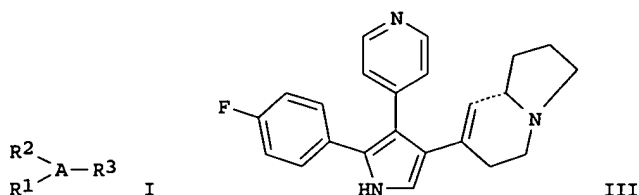
PRAI JP 2001-246344

A

20010815

OS MARPAT 138:204948

GI



AB Disclosed are pharmaceutical compns. for the prevention or treatment of diabetes, containing as the active ingredient compds. represented by the general formula (I), or pharmacol. acceptable salts, esters, or other derivs. thereof [wherein A = benzene, pyridine, pyridazine, pyrimidine, pyrrole, furan, thiophene, pyrazole, imidazole, isoxazole, or isothiazole, each being optionally substituted; R1 = aryl or heteroaryl, each being optionally substituted; R2 = optionally substituted nitrogenous heteroaryl; and R3 = a mono- or poly-cyclic nitrogenous heterocycle which may be substituted, i.e. Q-Q3 [wherein a bond accompanied by a dotted line represents a single or a double bond; m = 1,2; n = 1-3; one of D and E is N and the other is (un)substituted CH; one of D1 and E1 is (un)substituted NH and the other is (un)substituted CH; R5 = H, HO, NO2, cyano, halo, lower alkoxy, halo-lower alkoxy, lower alkylthio, halo-lower alkylthio, (un)substituted NH2, lower alkyl, lower alkenyl, or lower alkynyl, aralkyl, cycloalkyl, oxo, hydroxyamino, lower alkoxyimino, lower alkylene, lower alkylenedioxy, lower alkylsulfinyl, lower alkylsulfonyl, (un)substituted aryl, aryloxy, lower alkylidene, or aralkylidene; R6 = H, HO, NO2, cyano, halo, lower (halo)alkoxy, lower (halo)alkylthio, (un)substituted NH2, lower alkyl, lower alkenyl, etc.], with the proviso that the A-constituent atoms to which R1 and R3 bonded are each adjacent to the A-constituent atom to which R2 is bonded]. These compds. inhibit the production of cytokines and are useful for the prevention and treatment of diabetes, in particular type I diabetes. Thus, 3.00 g 4-bromo-2-(4-fluorophenyl)-3-(pyridin-4-yl)-1-triisopropylsilyl-1H-pyrrole was dissolved in 60 mL THF, treated with 4.36 mL 1.6 M BuLi/hexane at -78°, stirred for 10 min, treated with 1.29 g (1R,8aS)-2-methoxy-1,2,3,5,6,7,8,8a-octahydroindolizin-7-one, stirred at -78° for 2 h and at room temperature for 1 h, poured into saturated aqueous NaHCO<sub>3</sub>, and extracted with EtOAc. The EtOAc extract was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure, and the residue was dissolved in 40 mL CH<sub>2</sub>Cl<sub>2</sub>, treated with 1.95 mL CF<sub>3</sub>CO<sub>2</sub>H, refluxed for 1 h, concentrated under reduced pressure.

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The residue was dissolved in 30 mL THF, treated with 25.3 mL 1 M Bu4NF/THF, and stirred at room temperature for 10 min to give, after workup, 22% 2-(4-fluorophenyl)-4-[(2R,8aS)-2-methoxy-1,2,3,5,8,8a-hexahydroindolizin-7-yl]-3-(pyridin-4-yl)-1H-pyrrole (II). One compound (III) at 90-130 mg/kg/day p.o. prevented by 90% the onset of diabetes induced by cyclophosphamide in NOD mice. Pharmaceutical formulations, e.g. a powder containing II, was prepared

IT 443685-11-8P 443685-12-9P 443685-13-0P

443685-14-1P 443685-15-2P 443685-18-5P

443685-19-6P 443685-20-9P 500007-66-9P

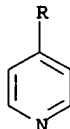
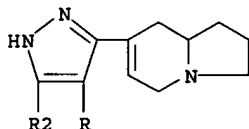
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of phenyl(hexahydroindoliziny)l(pyridinyl)pyrrole derivs. and related compds. as inhibitors of production of cytokines and for prevention and treatment of diabetes)

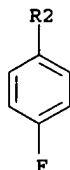
RN 443685-11-8 CAPLUS

CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,8,8a-hexahydro- (9CI) (CA INDEX NAME)

PAGE 1-A



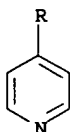
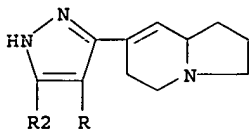
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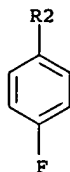
CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro- (9CI) (CA INDEX NAME)

PAGE 1-A



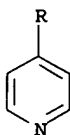
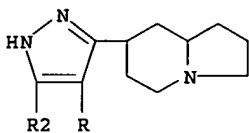


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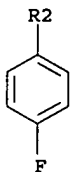


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 CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]octahydro- (9CI) (CA INDEX NAME)

PAGE 1-A

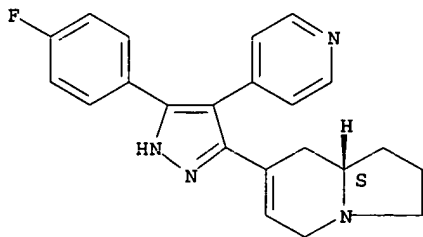


PAGE 2-A



RN 443685-14-1 CAPLUS  
 CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,8,8a-hexahydro-, (8aS)- (9CI) (CA INDEX NAME)

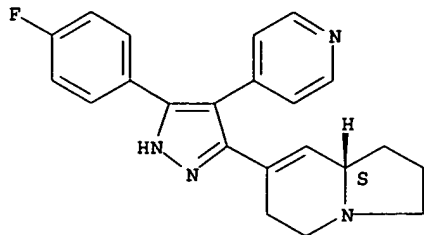
Absolute stereochemistry.



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Absolute stereochemistry.

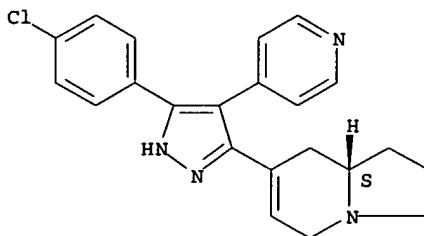
10/625024



RN 443685-18-5 CAPLUS

CN Indolizine, 7-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,8,8a-hexahydro-, (8aS)- (9CI) (CA INDEX NAME)

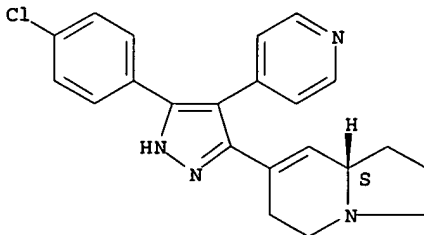
Absolute stereochemistry.



RN 443685-19-6 CAPLUS

CN Indolizine, 7-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro-, (8aS)- (9CI) (CA INDEX NAME)

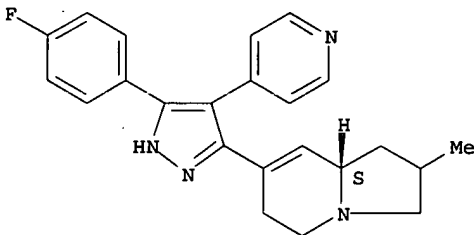
Absolute stereochemistry.



RN 443685-20-9 CAPLUS

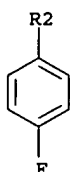
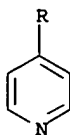
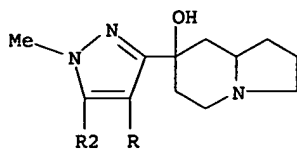
CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro-2-methyl-, (8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 500007-66-9 CAPLUS

CN 7-Indolizinol, 7-[5-(4-fluorophenyl)-1-methyl-4-(4-pyridinyl)-1H-pyrazol-3-yl]octahydro- (9CI) (CA INDEX NAME)



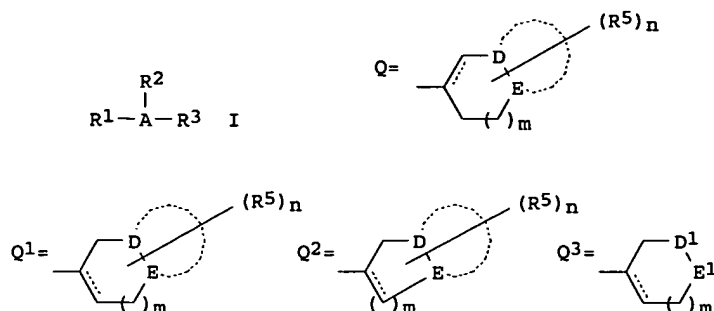
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2002:905860 CAPLUS  
DN 138:4600  
TI Preparation of heterocyclic compounds and pharmaceutical composition  
containing them for prevention or treatment of arthritis  
IN Ushiyama, Shigeru; Kimura, Tomio  
PA Sankyo Company, Limited, Japan  
SO PCT Int. Appl., 501 pp.  
CODEN: PIXXD2

DT Patent  
LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002094267	A1	20021128	WO 2002-JP5018	20020523
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2003040776	A2	20030213	JP 2002-149039	20020523
PRAI JP 2001-155032	A	20010524		
OS MARPAT 138:4600				
GI				



AB The invention relates to a pharmaceutical composition for prevention or treatment of arthritis such as chronic articular rheumatism and osteoarthritis which is useful in administering both a disease modifying antirheumatic drug (DMARD) and a compound represented by the general formula (I) or a pharmacol. acceptable salt, ester or other derivative thereof simultaneously, sep., or at a time interval [wherein A is a trivalent group derived from optionally substituted benzene, pyridine, pyridazine, pyrimidine, pyrrole, furan, thiophene, pyrazole, imidazole, isoxazole, or isothiazole; R1 is an optionally substituted aryl or heteroaryl; R2 is optionally substituted heteroaryl; and R3 is a group having the general formula Q-Q3 [wherein the bond accompanied by a dotted line represents a single or double bond; m is 1 or 2; R5 is hydrogen, HO, NO<sub>2</sub>, cyano, halo, lower alkoxy, lower haloalkoxy, lower alkylthio, etc.; n is 1 to 3; either D or E is nitrogen and the other is optionally substituted CH; one of D<sup>1</sup> and E<sup>1</sup> is optionally substituted NH and the other is optionally substituted CH<sub>2</sub>; and ring B containing D and E is a 4- to 7-membered heterocycle; provided that the constituent atoms of ring A to which R1 and R2 are bonded are each adjacent to the constituent atom of ring A to which R3 is bonded]]. Thus, 4.36 mL 1.6 M BuLi/hexane was added to a solution of 3.00 g 4-bromo-2-(4-fluorophenyl)-3-(pyridin-4-yl)-1-triisopropylsilyl-1H-pyrrole in 60 mL THF at -78° and stirred for 10 min, followed by adding 1.29 g (2R,8aS)-2-methoxy-1,2,3,5,6,7,8,8a-octahydroindolizin-7-one at -78°, and the resulting mixture stirred at -78° and at room temperature for 1 h to give, after workup and desilylation with Bu<sub>4</sub>NF in THF, 22% 2-(4-fluorophenyl)-4-[(2R,8aS)-2-methoxy-1,2,3,5,8,8a-hexahydroindolizin-7-yl]-3-(pyridin-4-yl)-1H-pyrrole (II). Pharmaceutical formulations, e.g. a powder containing II, were described. 2-(4-Fluorophenyl)-4-[(8aS)-1,2,3,5,8,8a-hexahydroindolizin-7-yl]-3-(pyridin-4-yl)-1H-pyrrole at 2 mg/kg p.o. and leflunomide at 1 mg/kg p.o. daily for 17 days inhibited the dead Mycobacterium butyricum (adjuvant)-induced arthritis in Lewis rats by 52.3% compared to 12.6 and 13.9% when II (R = H) at 2 mg/kg and leflunomide at 1 mg/kg were administered alone, resp.

IT 443685-10-7P 443685-11-8P 443685-12-9P  
443685-13-0P 443685-14-1P 443685-15-2P  
443685-18-5P 443685-19-6P 443685-20-9P  
443685-22-1P, 5-(3-Fluorophenyl)-3-(1,2,3,5,6,8a-hexahydroindolizin-7-yl)-4-(pyridin-4-yl)pyrazole 443685-23-2P,  
5-(4-Fluorophenyl)-3-(2-methyl-1,2,3,5,6,8a-hexahydroindolizin-7-yl)-4-(pyridin-4-yl)pyrazole 443685-24-3P, 5-(4-Fluorophenyl)-3-(2-phenyl-1,2,3,5,6,8a-hexahydroindolizin-7-yl)-4-(pyridin-4-yl)pyrazole 443685-30-1P, 5-(3-Chlorophenyl)-3-(1,2,3,5,6,8a-hexahydroindolizin-7-yl)-4-(pyridin-4-yl)pyrazole 443685-32-3P,  
5-(3,4-Difluorophenyl)-3-(1,2,3,5,6,8a-hexahydroindolizin-7-yl)-4-(pyridin-4-yl)pyrazole 443685-45-8P, 3-(2-Ethyl-1,2,3,5,6,8a-hexahydroindolizin-7-yl)-5-(4-fluorophenyl)-4-(pyridin-4-yl)pyrazole 443685-46-9P, 5-(4-Fluorophenyl)-3-(2-propyl-1,2,3,5,6,8a-hexahydroindolizin-7-yl)-4-(pyridin-4-yl)pyrazole 443685-48-1P,  
5-(4-Fluorophenyl)-3-(2-methylidene-1,2,3,5,6,8a-hexahydroindolizin-7-yl)-4-(pyridin-4-yl)pyrazole 443685-49-2P, 3-(2-Ethylidene-1,2,3,5,6,8a-hexahydroindolizin-7-yl)-5-(4-fluorophenyl)-4-(pyridin-4-yl)pyrazole 443685-50-5P, 5-(4-Fluorophenyl)-3-(2-propylidene-1,2,3,5,6,8a-hexahydroindolizin-7-yl)-4-(pyridin-4-yl)pyrazole 471864-51-4P, 3-(1,2,3,5,6,8a-Hexahydroindolizin-7-yl)-4-(pyridin-4-yl)-5-(3-trifluoromethylphenyl)pyrazole  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of heterocyclic compds. for prevention or treatment of arthritis in combination with disease modifying antirheumatic drug

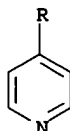
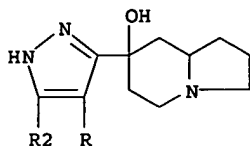
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(DMARD))

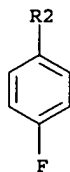
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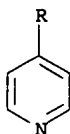
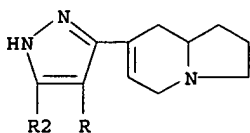
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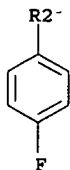
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PAGE 1-A



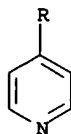
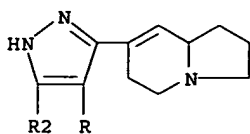
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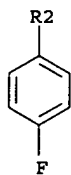
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PAGE 1-A

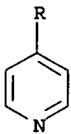
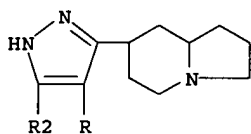


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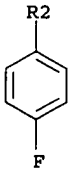


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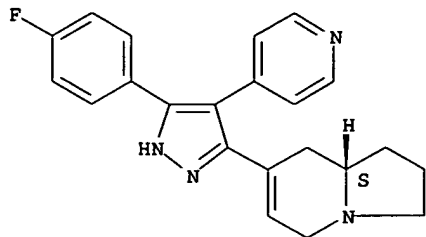
PAGE 2-A



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Absolute stereochemistry.

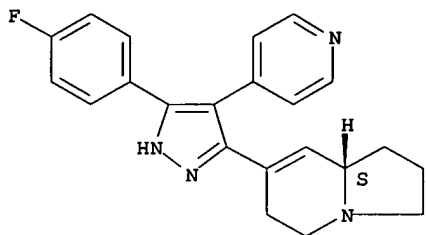
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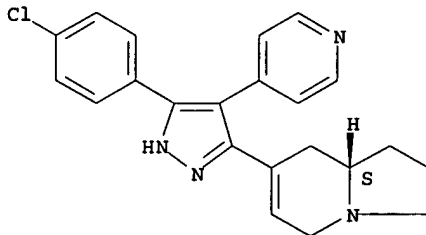
Absolute stereochemistry.



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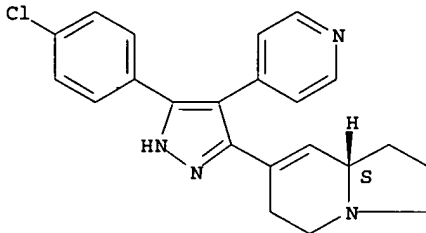
Absolute stereochemistry.



RN 443685-19-6 CAPLUS

CN Indolizine, 7-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro-, (8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

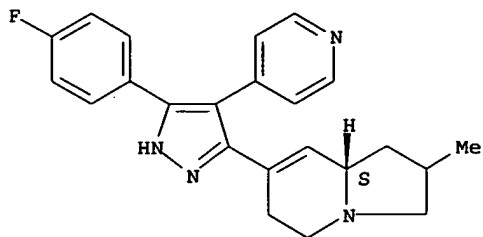


RN 443685-20-9 CAPLUS

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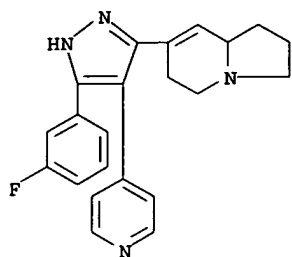
Absolute stereochemistry.

10/625024



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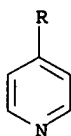
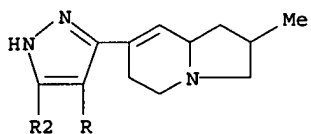
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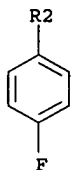
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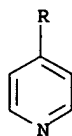
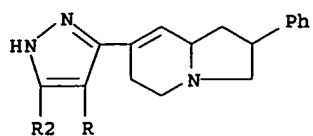


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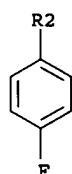
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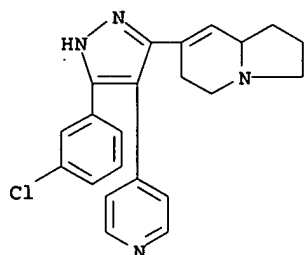
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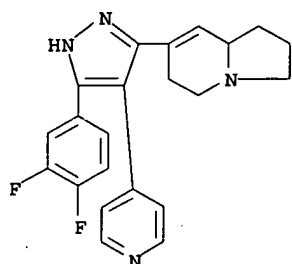
PAGE 2-A



RN 443685-30-1 CAPLUS  
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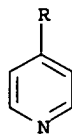
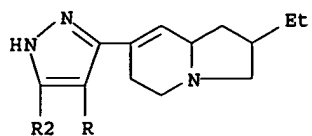


RN 443685-32-3 CAPLUS  
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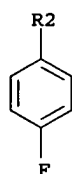


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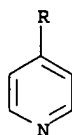
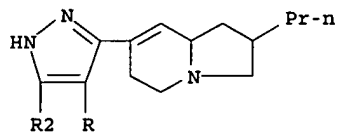


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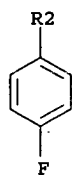


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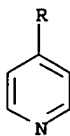
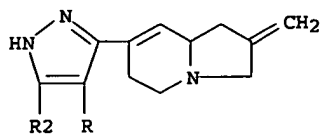


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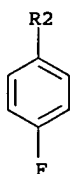


RN 443685-48-1 CAPLUS  
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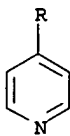
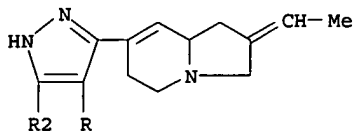


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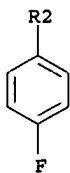


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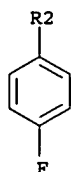
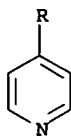
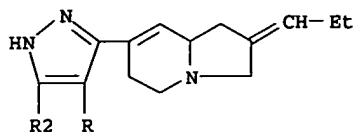
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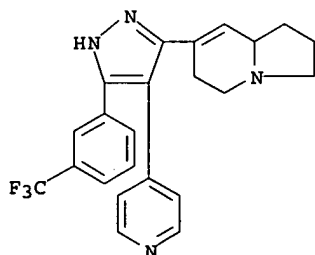
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RN 471864-51-4 CAPLUS  
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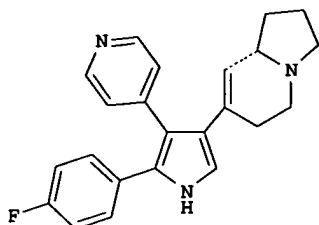


RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

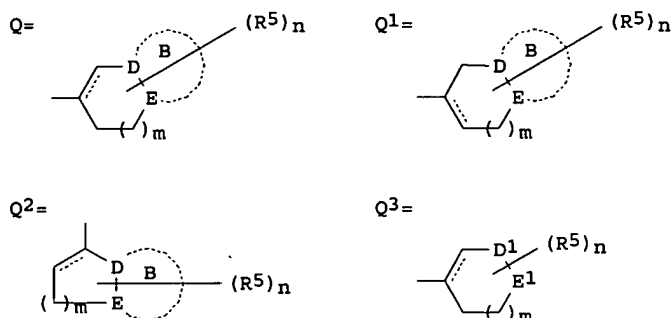
L15 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2002:793467 CAPLUS  
 DN 137:310916  
 TI Preparation of (hexahydroindolizidinyl)pyrrole, -thiophene, -pyrazole, and  
 -imidazole derivatives as cytokine production inhibitors and their novel  
 medicinal use in combination with nonsteroidal antiinflammatory agents  
 IN Ushiyama, Shigeru; Kimura, Tomio  
 PA Sankyo Company, Limited, Japan  
 SO PCT Int. Appl., 521 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080974	A1	20021017	WO 2002-JP3354	20020403
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,				

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 JP 2002363104 A2 20021218 JP 2002-101720 20020403  
 PRAI JP 2001-105615 A 20010404  
 OS MARPAT 137:310916  
 GI



II



AB Disclosed is a drug having relieved side effects of a nonsteroidal antiinflammatory agent (NSAID) which is to be used for simultaneously, sep., or intermittently during administering the nonsteroidal antiinflammatory agent, in particular having cyclooxygenase inhibitory activity, with an inflammatory cytokine production inhibitor. The active ingredient of the inflammatory cytokine production inhibitor is a compound represented by the general formula R1R2A-R3 [I; wherein A = an (un)substituted trivalent group selected from benzene, pyridine, pyridazine, pyrimidine, pyrrole, furan, thiophene, pyrazole, imidazole, isoxazole, and isothiazole; R1 = each (un)substituted aryl or heteroaryl; R2 = (un)substituted heteroaryl containing at least one N atom; R3 = Q-Q3; wherein m = 1,2; n = 1-3; R5 = H, HO, NO2, cyano, halo, lower alkoxy, halo-lower alkoxy, lower alkylthio, lower alkyl, lower alkenyl, lower alkynyl, aralkyl, oxo, hydroxyimino, lower alkoxyimino, lower alkylene, etc.; one of D and E is N and the other one is (un)substituted CH; one of D1 and E1 is (un)substituted NH and the other one is (un)substituted CH2; the ring B containing D and E = a 4- to 7-membered heterocyclic ring optionally fused with aryl, heteroaryl, cycloalkyl, or heterocyclyl group; a proviso is given]. The above compound alleviates the side effects, in particular stomach mucus membrane injury such as erosion or ulcer, of NSAID having cyclooxygenase inhibitory activity such as Aspirin, Etodolac, Diclofenac sodium, Aceclofenac, Indometacin, Farnesol, Nabumetone, Ibuprofen, Ketoprofen, Loxoprofen sodium, Naproxen, Nimesulide, Oxaprozin, Zaltoprofen, Piroxicam, Lornoxicam, Meloxicam, Celecoxib, Rofecoxib, Valdecoxib, and Etoricoxib. The above drug is useful for prevention or treatment of inflammations, malignant tumors, Alzheimer's disease, chronic articular rheumatism, or arthritis. Thus, 1-(4-fluorophenyl)-3-(4-pyridyl)-4-(1,2,3,5,6,8a-hexahydroindolizin-7-yl)pyrrole (II) at 30 mg/kg inhibited by 91% the injury of stomach mucous membrane induced by Diclofenac sodium (15 mg/kg) in rats. A powder, a granule, and a capsule containing the specific compound I were described.

IT 443685-10-7P 443685-11-8P 443685-12-9P  
 443685-13-0P 443685-14-1P 443685-15-2P  
 443685-18-5P 443685-19-6P 443685-20-9P  
 443685-22-1P, 5-(3-Fluorophenyl)-3-(1,2,3,5,6,8a-hexahydroindolizin-7-yl)-4-(pyridin-4-yl)pyrazole 443685-23-2P,  
 5-(4-Fluorophenyl)-3-(2-methyl-1,2,3,5,6,8a-hexahydroindolizin-7-yl)-4-(pyridin-4-yl)pyrazole 443685-24-3P, 5-(4-Fluorophenyl)-3-(2-

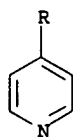
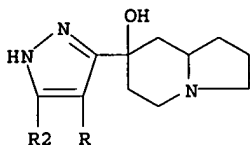
phenyl-1,2,3,5,6,8a-hexahydroindolizin-7-yl)-4-(pyridin-4-yl)pyrazole  
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 5-(3,4-Difluorophenyl)-3-(1,2,3,5,6,8a-hexahydroindolizin-7-yl)-4-(pyridin-4-yl)pyrazole 443685-45-8P, 3-(2-Ethyl-1,2,3,5,6,8a-hexahydroindolizin-7-yl)-5-(4-fluorophenyl)-4-(pyridin-4-yl)pyrazole  
 443685-46-9P, 5-(4-Fluorophenyl)-3-(2-propyl-1,2,3,5,6,8a-hexahydroindolizin-7-yl)-4-(pyridin-4-yl)pyrazole 443685-48-1P,  
 5-(4-Fluorophenyl)-3-(2-methylidene-1,2,3,5,6,8a-hexahydroindolizin-7-yl)-4-(pyridin-4-yl)pyrazole 443685-49-2P, 3-(2-Ethylidene-1,2,3,5,6,8a-hexahydroindolizin-7-yl)-5-(4-Fluorophenyl)-4-(pyridin-4-yl)pyrazole 443685-50-5P, 5-(4-Fluorophenyl)-3-(2-propylidene-1,2,3,5,6,8a-hexahydroindolizin-7-yl)-4-(pyridin-4-yl)pyrazole  
 471864-51-4P, 3-(1,2,3,5,6,8a-Hexahydroindolizin-7-yl)-4-(pyridin-4-yl)-5-(3-trifluoromethylphenyl)pyrazole  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of (hexahydroindolizinyl)heterocyclic compound derivs. as inflammatory cytokine production inhibitors and their medicinal use in combination with nonsteroidal antiinflammatory agents)

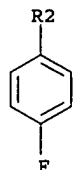
RN 443685-10-7 CAPLUS

CN 7-Indolizinol, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]octahydro- (9CI) (CA INDEX NAME)

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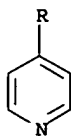
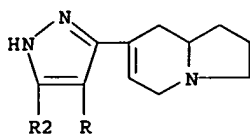
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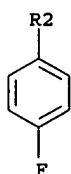
RN 443685-11-8 CAPLUS

CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,8,8a-hexahydro- (9CI) (CA INDEX NAME)

PAGE 1-A

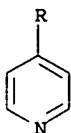
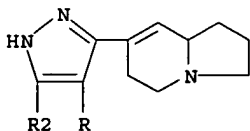


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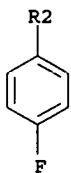


RN 443685-12-9 CAPLUS  
CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-  
1,2,3,5,6,8a-hexahydro- (9CI) (CA INDEX NAME)

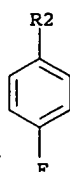
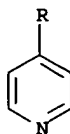
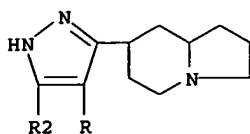
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PAGE 2-A



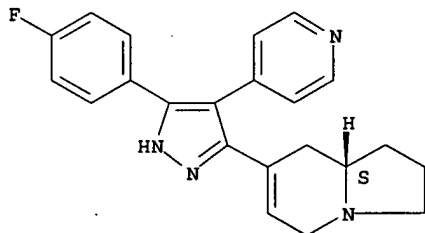
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CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]octahydro- (9CI) (CA INDEX NAME)



RN 443685-14-1 CAPLUS

CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,8,8a-hexahydro-, (8aS)-(9CI) (CA INDEX NAME)

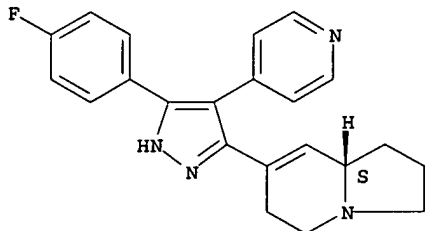
Absolute stereochemistry.



RN 443685-15-2 CAPLUS

CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro-, (8aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



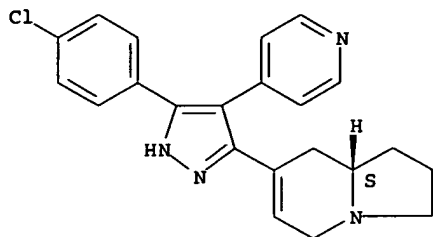
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CN Indolizine, 7-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,8,8a-hexahydro-, (8aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



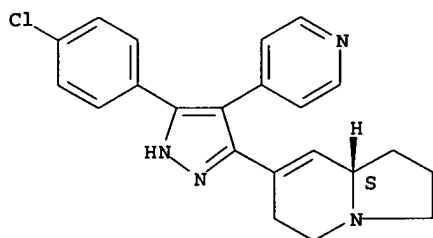
10/625024



RN 443685-19-6 CAPLUS

CN Indolizine, 7-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro-, (8aS)- (9CI) (CA INDEX NAME)

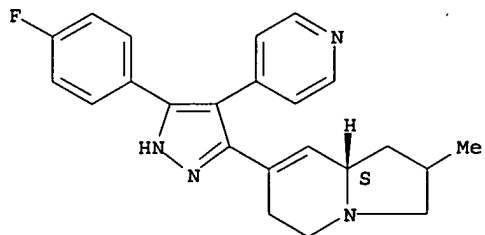
Absolute stereochemistry.



RN 443685-20-9 CAPLUS

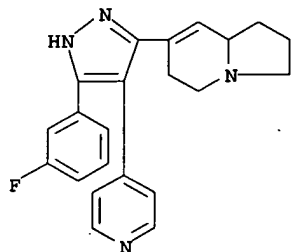
CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro-2-methyl-, (8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 443685-22-1 CAPLUS

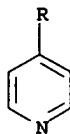
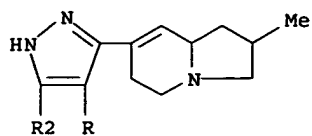
CN Indolizine, 7-[5-(3-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro- (9CI) (CA INDEX NAME)



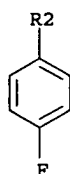
RN 443685-23-2 CAPLUS

CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro-2-methyl- (9CI) (CA INDEX NAME)

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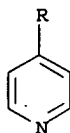
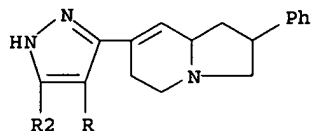


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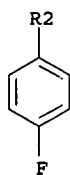


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 1,2,3,5,6,8a-hexahydro-2-phenyl- (9CI) (CA INDEX NAME)

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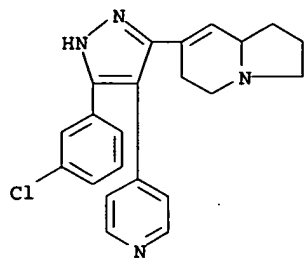


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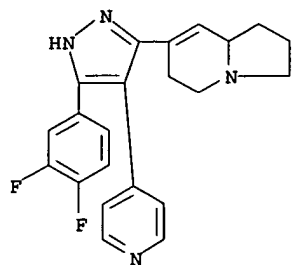


RN 443685-30-1 CAPLUS  
 CN Indolizine, 7-[5-(3-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-  
 1,2,3,5,6,8a-hexahydro- (9CI) (CA INDEX NAME)

10/625024

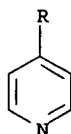
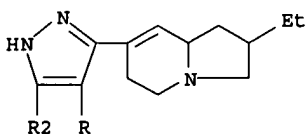


RN 443685-32-3 CAPLUS  
CN Indolizine, 7-[5-(3,4-difluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-  
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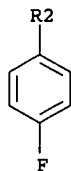


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CN Indolizine, 2-ethyl-7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-  
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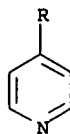
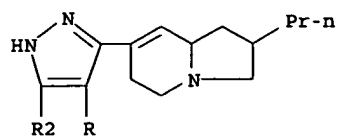


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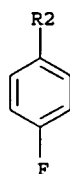


RN 443685-46-9 CAPLUS  
CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-  
1,2,3,5,6,8a-hexahydro-2-propyl- (9CI) (CA INDEX NAME)

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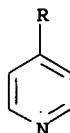
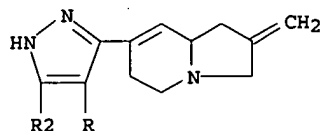


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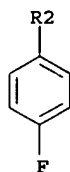


RN 443685-48-1 CAPLUS  
 CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-  
 1,2,3,5,6,8a-hexahydro-2-methylene- (9CI) (CA INDEX NAME)

PAGE 1-A

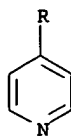
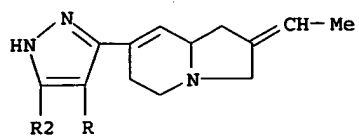


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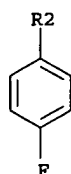


RN 443685-49-2 CAPLUS  
 CN Indolizine, 2-ethylidene-7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-  
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PAGE 1-A

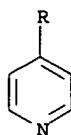
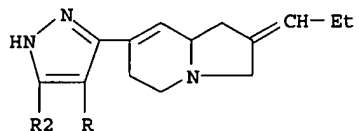


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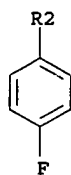


RN 443685-50-5 CAPLUS  
 CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-  
 1,2,3,5,6,8a-hexahydro-2-propylidene- (9CI) (CA INDEX NAME)

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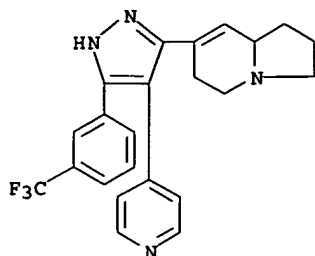


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RN 471864-51-4 CAPLUS  
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10/625024



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:591913 CAPLUS

DN 137:150215

TI Cdk4 and/or Cdk6 inhibitors with biaryl ureas and their salts as antitumor agents

IN Hatayama, Satoshi; Hayashi, Kyoko; Honma, Mitsuki; Takahashi, Ikuko

PA Banyu Pharmaceutical Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 194 pp.

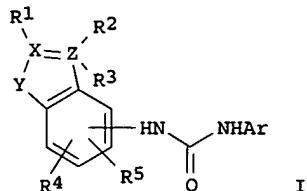
CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2002220338	A2	20020809	JP 2001-18755	20010126
PRAI	JP 2001-18755		20010126		
OS	MARPAT 137:150215				
GI					



AB This invention relates to the general structures (I; Ar = N-containing hetero aromatic ring, X, Z = C, etc.; Y = CO, etc.; R1-R5 = H, etc.) and their salts as Cdk4 and/or Cdk6 inhibitors. I have antiproliferative effects on cancer cells and are potential antitumor agents. Formulation examples of I capsules, tablets, and injections were given.

IT 322685-65-4 322689-29-2

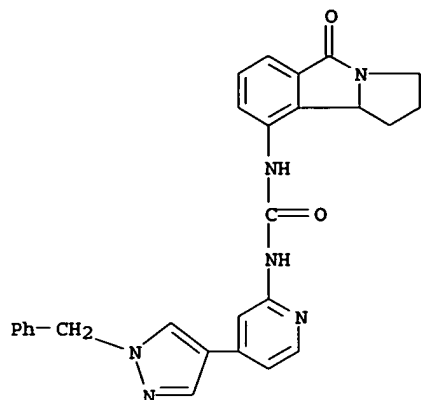
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Cdk4 and/or Cdk6 inhibitors with biaryl ureas and their salts as antitumor agents)

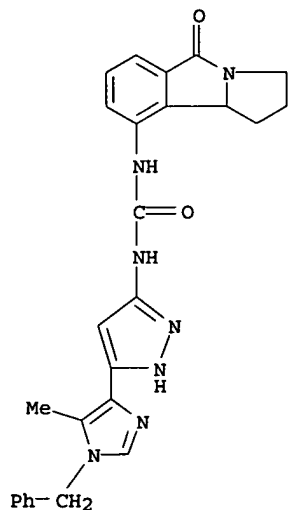
RN 322685-65-4 CAPLUS

CN Urea, N-[4-[1-(phenylmethyl)-1H-pyrazol-4-yl]-2-pyridinyl]-N'-(2,3,5,9b-tetrahydro-5-oxo-1H-pyrrolo[2,1-a]isoindol-9-yl)-(9CI) (CA INDEX NAME)

10/625024



RN 322689-29-2 CAPLUS  
 CN Urea, N-[5-[5-methyl-1-(phenylmethyl)-1H-imidazol-4-yl]-1H-pyrazol-3-yl]-  
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 INDEX NAME)

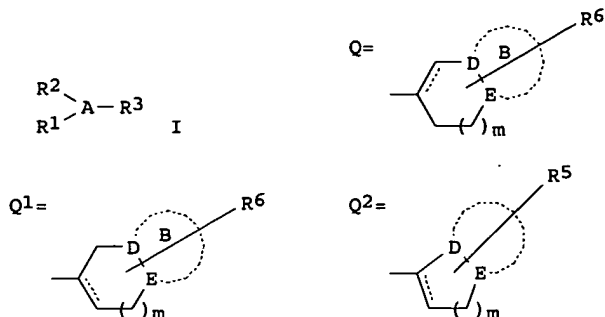


L15 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2002:555493 CAPLUS  
 DN 137:125158  
 TI Preparation of compounds substituted with bicyclic amino groups as  
 inhibitors of production of inflammatory cytokines  
 IN Kimura, Tomio; Aoki, Kazumasa; Nakao, Akira  
 PA Sankyo Company, Limited, Japan  
 SO PCT Int. Appl., 300 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002057265	A1	20020725	WO 2002-JP402	20020122
	W: AU, BR, CA, CN, CO, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PH, PL, RU, SG, SK, US, VN, ZA				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	JP 2002284782	A2	20021003	JP 2002-10923	20020121
	EP 1361225	A1	20031112	EP 2002-716325	20020122
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
	US 2004147525	A1	20040729	US 2003-625024	20030722
PRAI	JP 2001-12881	A	20010122		

*this app*

JP 2001-13590 A 20010122  
 WO 2002-JP402 W 20020122  
 OS MARPAT 137:125158  
 GI



AB Provided are compds. represented by the general formula (I) or pharmacol. acceptable salts, esters or other derivs. thereof [wherein A = benzene having 3 R4 groups, pyridine having 2 R4 groups, pyrimidine, furan, thiophene, pyrazole, imidazole, isoxazole, or isothiazole each having R4 group; wherein R4 = H, (un)substituted lower alkyl, (un)substituted lower alkenyl, (un)substituted lower alkynyl, aralkyl, (un)substituted substituted cycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl; R1 = (un)substituted aryl or heteroaryl; R2 = (un)substituted heteroaryl having at least one n atom; R3 = Q, Q1, or Q2; wherein m = 1,2; R5 = H, OH, NO2, cyano, halo, lower alkoxy, lower haloalkoxy, lower alkylthio, lower haloalkylthio, (un)substituted NH2, N-heterocyclyl, (un)substituted lower alkyl, (un)substituted lower alkenyl, (un)substituted lower alkynyl, aralkyl, etc.; one of D and E is (un)substituted CH; B = (un)saturated to 7-membered ring heterocyclic ring]. These compds. are capable of inhibiting the production of inflammatory cytokines and useful as preventives and/or remedies of inflammatory cytokines-mediated diseases such chronic articular rheumatism and osteoarthritis and as antiinflammatory agents and analgesics. Thus, 10.1 g  $\alpha$ -(p-toluenesulfonyl)-4-fluorobenzyl isocyanide and 8.0 g ( $\pm$ )-7-(4-pyridylmethyleneamino)-1,2,3,5,6,7,8a-octahydroisindolidine were dissolved in 150 mL CH2Cl2, followed by adding 5.22 mL 1,8-diazabicyclo[5.4.0]-7-undecene, and the resulting mixture was stirred at room temperature for 2 h to give 14% ( $\pm$ )-4-(4-fluorophenyl)-5-(pyridin-4-yl)-1-(1,2,3,5,6,7,8,8a-octahydroisindolidin-7-yl)imidazole (II). 5-(4-Fluorophenyl)-3-[(8aS)-2-methyl-1,2,3,5,6,8a-hexahydroindolidin-7-yl]-4-(pyridin-4-yl)pyrazole in vitro inhibited the production of tumor necrosis factor  $\alpha$  (TNF $\alpha$ ) with IC50 of 0.0026  $\mu$ M in whole human blood. Pharmaceutical formulations, e.g. a dispersant formulation containing I, were described.

IT 443685-10-7P 443685-11-8P 443685-12-9P  
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 443685-53-8P 443685-54-9P 443685-55-0P  
 443685-56-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of compds. substituted with bicyclic amino groups as inhibitors of production of inflammatory cytokines as preventives and/or remedies of inflammatory cytokines-mediated diseases)

RN 443685-10-7 CAPLUS

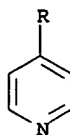
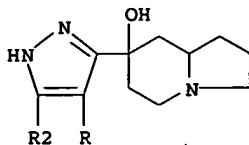
CN 7-Indolizinol, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-



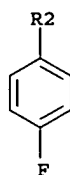
10/625024

yl]octahydro- (9CI) (CA INDEX NAME)

PAGE 1-A

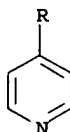
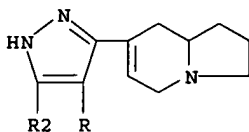


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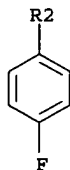


RN 443685-11-8 CAPLUS  
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1,2,3,5,8,8a-hexahydro- (9CI) (CA INDEX NAME)

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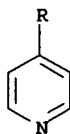
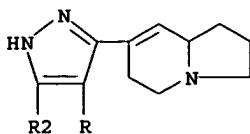


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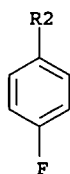


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1,2,3,5,6,8a-hexahydro- (9CI) (CA INDEX NAME)

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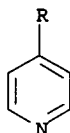
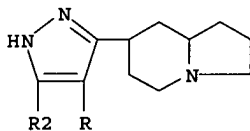


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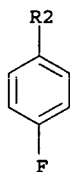


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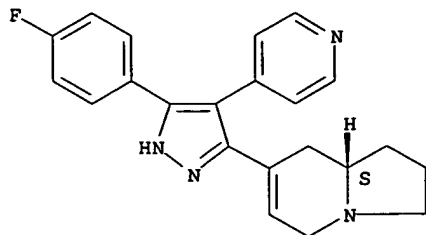
PAGE 2-A



RN 443685-14-1 CAPLUS  
 CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,8,8a-hexahydro-, (8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

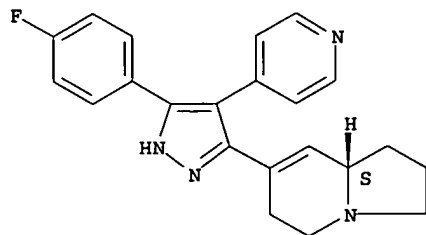
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RN 443685-15-2 CAPLUS

CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro-, (8aS)-(9CI) (CA INDEX NAME)

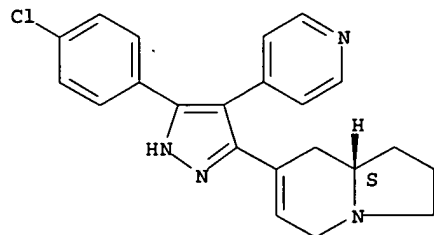
Absolute stereochemistry.



RN 443685-18-5 CAPLUS

CN Indolizine, 7-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,8,8a-hexahydro-, (8aS)-(9CI) (CA INDEX NAME)

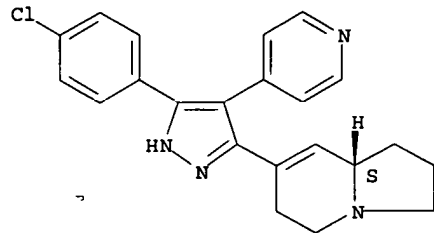
Absolute stereochemistry.



RN 443685-19-6 CAPLUS

CN Indolizine, 7-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro-, (8aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

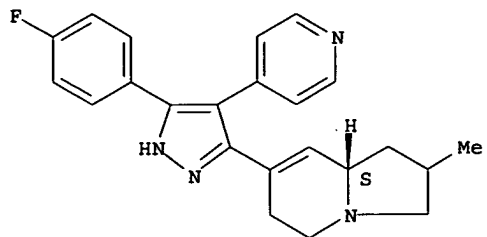


RN 443685-20-9 CAPLUS

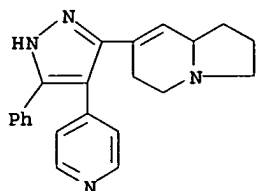
CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro-2-methyl-, (8aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

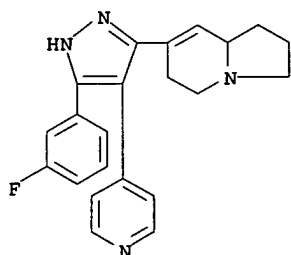
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RN 443685-21-0 CAPLUS  
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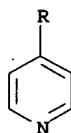
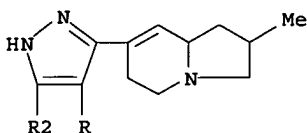


RN 443685-22-1 CAPLUS  
CN Indolizine, 7-[5-(3-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro- (9CI) (CA INDEX NAME)

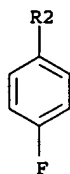


RN 443685-23-2 CAPLUS  
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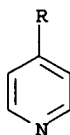
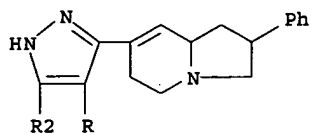


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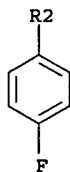


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 1,2,3,5,6,8a-hexahydro-2-phenyl- (9CI) (CA INDEX NAME)

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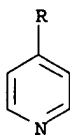
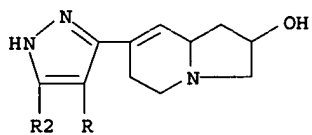


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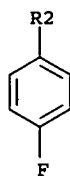


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 1,2,3,5,6,8a-hexahydro- (9CI) (CA INDEX NAME)

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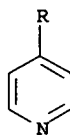
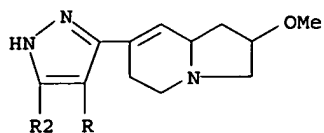


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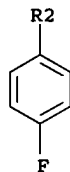


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1,2,3,5,6,8a-hexahydro-2-methoxy- (9CI) (CA INDEX NAME)

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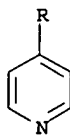
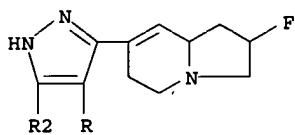


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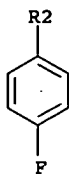


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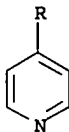
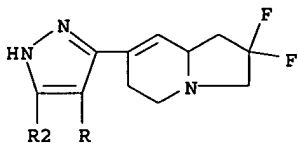


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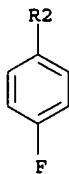


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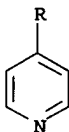
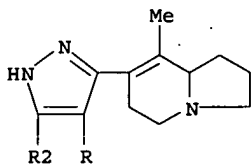


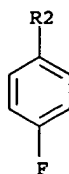
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RN 443685-29-8 CAPLUS  
CN Indolizine, 7-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro-8-methyl- (9CI) (CA INDEX NAME)

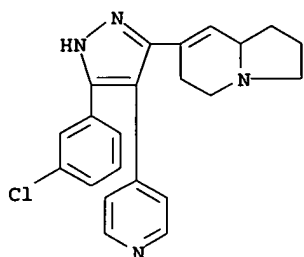
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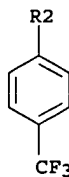
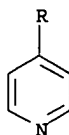
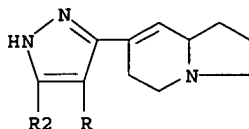
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RN 443685-31-2 CAPLUS

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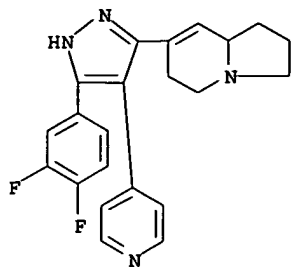


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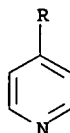
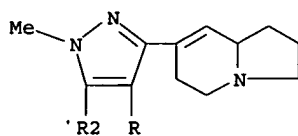
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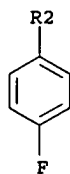
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CN Indolizine, 7-[5-(4-fluorophenyl)-1-methyl-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2,3,5,6,8a-hexahydro- (9CI) (CA INDEX NAME)

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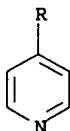
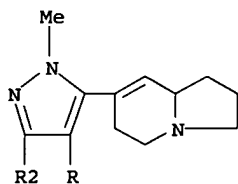
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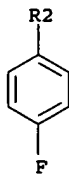
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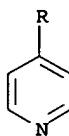
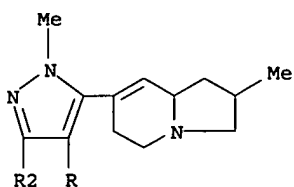


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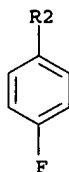


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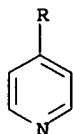
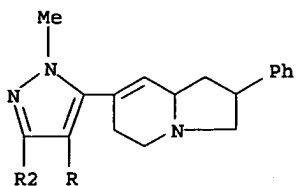


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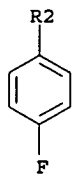


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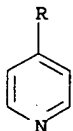
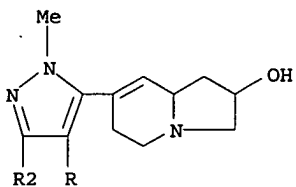


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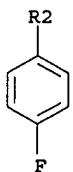


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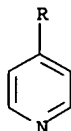
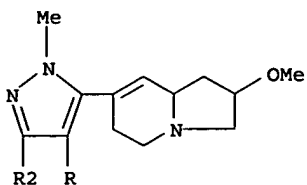


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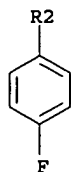
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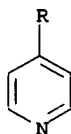
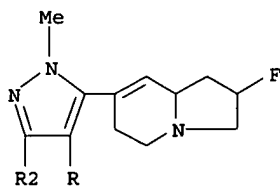
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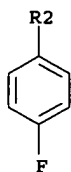
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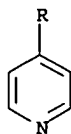
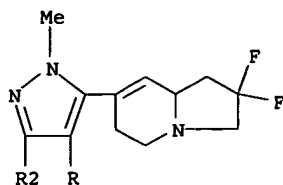


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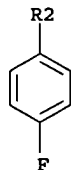
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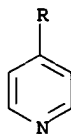
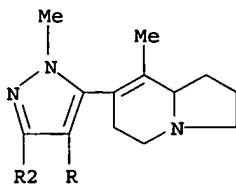
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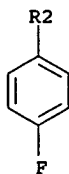
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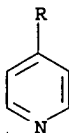
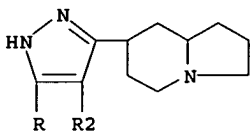


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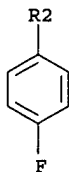


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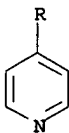
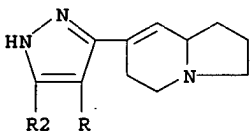


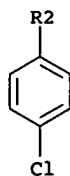
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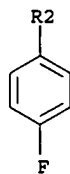
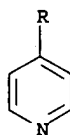
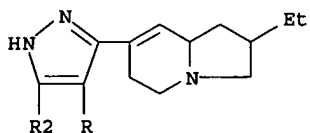
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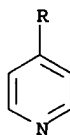
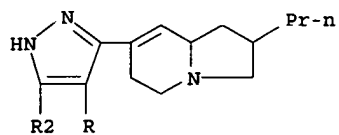




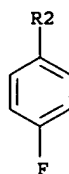
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1,2,3,5,6,8a-hexahydro- (9CI) (CA INDEX NAME)



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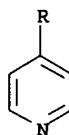
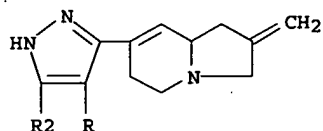


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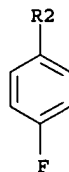


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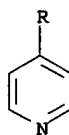
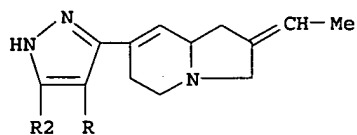


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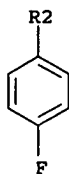
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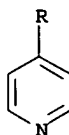
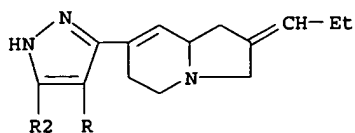


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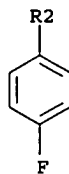


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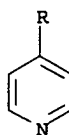
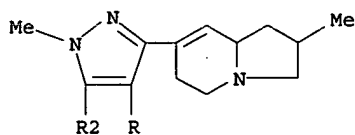


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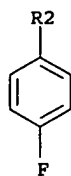


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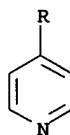
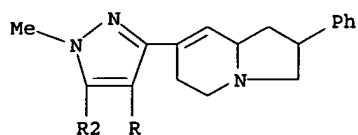


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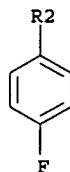


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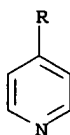
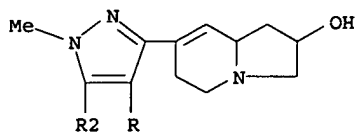


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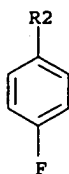


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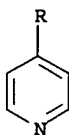
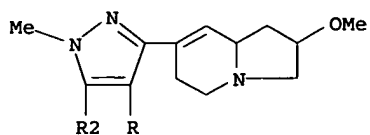


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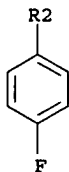


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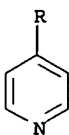
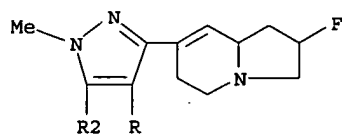


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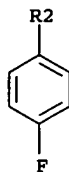


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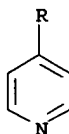
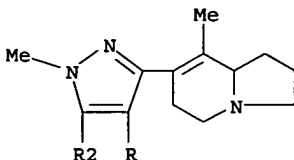


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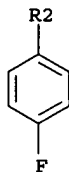


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RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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AN 2001:78363 CAPLUS

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TI Preparation of N,N'-biarylurea derivatives as inhibitors of cyclin-dependent kinases (Cdk4 and Cdk6)

IN Hayama, Takashi; Hayashi, Kyoko; Honma, Mitsutaka; Takahashi, Ikuko

PA Banyu Pharmaceutical Co., Ltd., Japan

SO PCT Int. Appl., 460 pp.

CODEN: PIXXD2

DT Patent

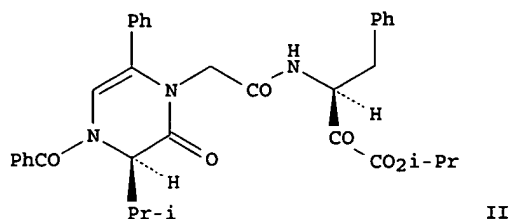
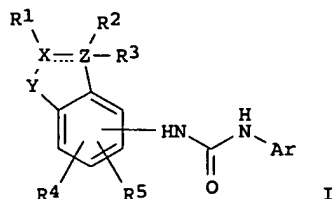
LA Japanese

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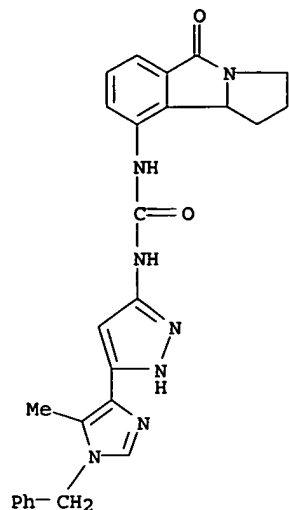
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 OS MARPAT 134:147614  
 GI



AB N-(hetero)aryl-N'-heterocyclylurea derivs. represented by general formula (I) [wherein Ar represents a nitrogenous heterocyclic aromatic group such as (un)substituted pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, pyrrolyl, imidazolyl, indolyl, isoindolyl, quinolyl, isoquinolyl, benzothiazolyl, or benzoxazolyl; X and Z each represents C or N or together with R1 or R2 and/or R3 represent CH or N; Y represents CO, SO, or SO2; R1 represents hydrogen, (un)substituted lower alkyl, Y3-W2-Y4-R5, etc.; wherein R5 = H, (un)substituted lower alkyl, lower alkenyl, lower alkynyl, lower cycloalkyl, aryl, imidazolyl, isoxazolyl, isoquinolyl, isoindolyl, indazolyl, indolyl, indolidinyl, isothiazolyl, ethylenedioxyphenyl, oxazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, pyrazolyl, quinoxalinyl, quinolyl, etc.; W2 = single bond, O, S, SO, SO2, N-(un)substituted NH, SO2NH, NHSO2NH, NHSO2, CONH, NHCO, NHCONH, NHCO2, etc.; Y3, Y4 = single bond, linear or branched lower alkylene; R2 and R3 each represents hydrogen, lower alkyl or alkoxy, or Y3-W2-Y4-R5 (Y3, W2, Y4, R5 = same as above), or one of R2 and R3 together with R1 and X forms cyclohexane, cyclopentane, piperidine, 3,4,5,6-tetrahydro-1,3-oxazine, tetrahydrothiopyran, pyrrolidine, tetrahydrothiofuran, oxazolidine ring, etc.; R4 and R5 represent H, halo, OH, amino, or Y3-W2-Y4-R5 (Y3, W2, Y4, R5 = same as above)] or salts thereof are prepared. The compds. (e.g. II) have a remarkable proliferation-inhibitory effect on tumor cells. A Cdk4 and/or Cdk6 inhibitor for use in the therapy of malignant tumor can hence be provided. II showed IC50 of 0.061 and 0.019  $\mu$ M against cyclin-D1-Cdk4 and cyclin-D2-Cdk4, resp., vs. 0.36 and 0.056  $\mu$ M, resp., for (+)-flavopiridol, and inhibited the proliferation of HCT116 and MKN-1 cells with IC50 of 0.013 and 0.10  $\mu$ M, resp., vs. 0.15 and 0.87  $\mu$ M, resp., for (+)-flavopiridol. Pharmaceutical formulations containing I were prepared

IT 322689-29-2P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of N-(hetero)aryl-N'-heterocyclylurea derivs. as in inhibitors of cyclin-dependent kinases (Cdk4 and Cdk6) and antitumor agents)

RN 322689-29-2 CAPLUS  
 CN Urea, N-[5-[5-methyl-1-(phenylmethyl)-1H-imidazol-4-yl]-1H-pyrazol-3-yl]-N'-(2,3,5,9b-tetrahydro-5-oxo-1H-pyrrolo[2,1-a]isoindol-9-yl)- (9CI) (CA INDEX NAME)

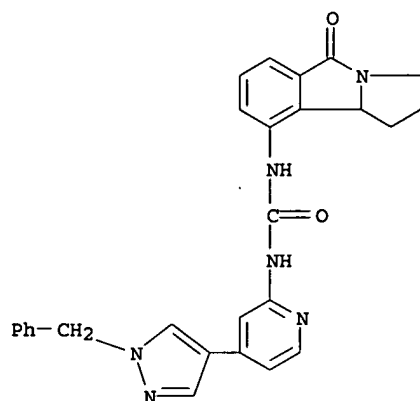


IT 322685-65-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of N-(hetero)aryl-N'-heterocyclurea derivs. as inhibitors of cyclin-dependent kinases (Cdk4 and Cdk6) and antitumor agents)

RN 322685-65-4 CAPLUS

CN Urea, N-[4-[1-(phenylmethyl)-1H-pyrazol-4-yl]-2-pyridinyl]-N'-(2,3,5,9b-tetrahydro-5-oxo-1H-pyrrolo[2,1-a]isoindol-9-yl)- (9CI) (CA INDEX NAME)



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:580564 CAPLUS

DN 125:328525

TI Substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA antagonists useful for the treatment of neurodegenerative disorders or neurotoxic injuries

IN Dehaven-Hudkins, Diane L.; Dority, John A., Jr.; Earley, William G.; Kumar, Virendra; Mallamo, John P.; Miller, Matthew S.; Subramanyam, Chakrapani

PA Sterling Winthrop Inc., USA

SO U.S., 80 pp., Cont.-in-part of U.S. Ser. No. 121,127, abandoned.  
CODEN: USXXAM

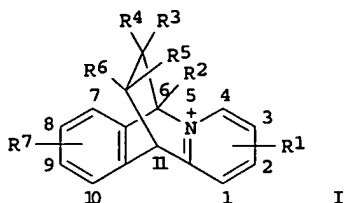
DT Patent

LA English

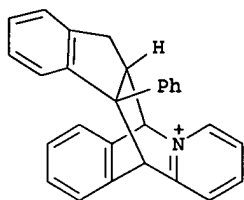
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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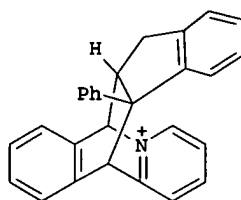
EP 656359	A1	19950607	EP 1994-202601	19940910
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2131966	AA	19950315	CA 1994-2131966	19940913
AU 9472940	A1	19950330	AU 1994-72940	19940913
AU 683679	B2	19971120		
HU 68530	A2	19950628	HU 1994-2634	19940914
JP 07179462	A2	19950718	JP 1994-220255	19940914
US 5631264	A	19970520	US 1995-449125	19950524
PRAI US 1993-121127	B2	19930914		
US 1994-283317	A	19940729		
OS MARPAT 125:328525				
GI				



I



II



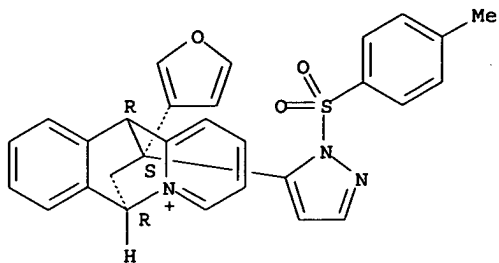
III

- AB Substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts I. (X-)p are claimed, wherein: R1 is hydrogen, or from one to four, the same or different, substituents in any of the 1, 2, 3, or 4 positions selected from the group consisting of, e.g., lower alkoxy, lower alkyl, halogen, hydroxy; R2 is hydrogen, lower alkyl, cyano or lower-alkoxycarbonyl; R3 and R4 are independently hydrogen, or lower alkyl; or R3 and R4 together form a cycloalkyl ring, or a lower alkylidene group; R5 and R6 are independently hydrogen, Ph, furyl or benzofuryl; or R3 and R5, and/or R4 and R6 taken together with the carbon atoms to which they are attached form a bicyclic ring system; R7 is hydrogen, or from one to four, the same or different, substituents in any of the 7, 8, 9, or 10 positions selected from the group consisting of, e.g., lower alkyl, lower alkanoyloxy, halogen, nitro, hydroxy, lower alkoxy, methylenedioxy; X- is an anion; and, p is zero when R7 is a neg. charged radical and p is one when R7 is other than a neg. charged radical (with provisos); or pharmaceutical compns. containing them for the treatment of neurodegenerative disorders or neurotoxic injuries. Thus, e.g., treatment of 1-indanone with PhLi followed by acid afforded 3-phenyl-1H-indene; 2-pyridinecarboxaldehyde was converted to its ethylene acetal [2-(1,3-dioxolan-2-yl)pyridine], and the latter alkylated with benzyl bromide to afford 2-(1,3-dioxolan-2-yl)-1-benzylpyridinium bromide; cyclization of the latter followed by anion exchange afforded benzo[b]quinolizinium hexafluorophosphate; finally, cycloaddn. reaction of the latter with 3-phenyl-1H-indene afforded an isomeric mixture of 6,11[[2',3']-3'-phenylindanyl]6,11-dihydrobenzo[b]quinolizinium hexafluorophosphate (II/III.PF6-) which exhibited binding to the PCP receptor with  $K_i = 7.58$  nM. Data were also presented for antagonism by I of NMDA-induced neurotoxicity in cultured neurons as well as for the protection effect of I in a rat ischemia model.
- IT 170485-95-7P 170486-26-7P 170714-64-4P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA antagonists useful for the treatment of neurodegenerative disorders or neurotoxic injuries)
- RN 170485-95-7 CAPLUS
- CN 6,11-Ethanobenzo[b]quinolizinium, 12-(3-furanyl)-6,11-dihydro-12-[1-[(4-methylphenyl)sulfonyl]-1H-pyrazol-5-yl]-, bromide,

10/625024

(6 $\alpha$ ,11 $\alpha$ ,12S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● Br<sup>-</sup>

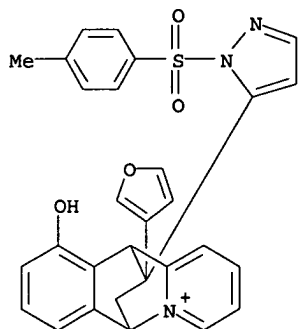
RN 170486-26-7 CAPLUS

CN 6,11-Ethanobenzo[b]quinolizinium, 12-(3-furanyl)-6,11-dihydro-10-hydroxy-12-[1-[(4-methylphenyl)sulfonyl]-1H-pyrazol-5-yl]-, (6 $\alpha$ ,11 $\alpha$ ,12S\*)-, perchlorate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 170486-25-6

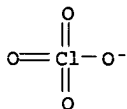
CMF C29 H24 N3 O4 S



CM 2

CRN 14797-73-0

CMF Cl O4



RN 170714-64-4 CAPLUS

CN 6,11-Ethanobenzo[b]quinolizinium, 12-(3-furanyl)-6,11-dihydro-12-[1-[(4-methylphenyl)sulfonyl]-1H-pyrazol-5-yl]-, bromide, (6 $\alpha$ ,11 $\alpha$ ,12R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



The chemical structure shows a complex molecule. At the top, a 4-methylphenyl group is connected to a sulfonamide group (-SO<sub>2</sub>-N-). The nitrogen of the sulfonamide is connected to a pyrrole ring. The pyrrole ring is further connected to a complex polycyclic system. This system includes a benzene ring with a hydroxyl group (-OH), a five-membered ring with an oxygen atom, and a quaternary nitrogen atom (N<sup>+</sup>) within a polycyclic framework.

$$\begin{array}{c} \text{O} \\ || \\ \text{O}=\text{Cl}-\text{O}^- \\ || \\ \text{O} \end{array}$$

IT 170486-57-4P 170486-83-6P 170486-90-5P  
170486-97-2P 170487-19-1P 170487-29-3P  
170487-34-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as  
NMDA antagonists useful for the treatment of neurodegenerative  
disorders or neurotoxic injuries)

10/625024

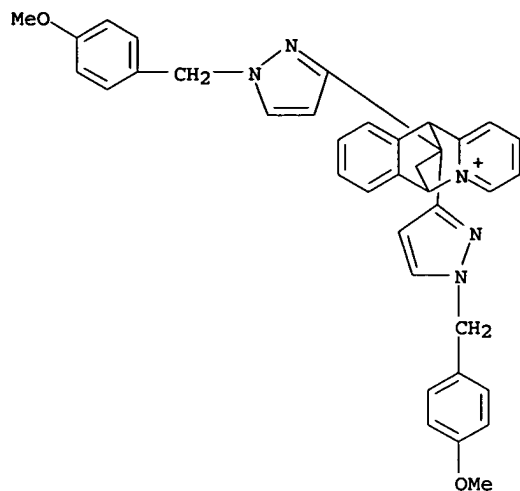
RN 170486-57-4 CAPLUS

CN 6,11-Ethanobenzo[b]quinolizinium, 6,11-dihydro-12,12-bis[1-[(4-methoxyphenyl)methyl]-1H-pyrazol-3-yl]-, perchlorate (9CI) (CA INDEX NAME)

CM 1

CRN 170486-56-3

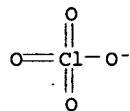
CMF C37 H34 N5 O2



CM 2

CRN 14797-73-0

CMF Cl O4



RN 170486-83-6 CAPLUS

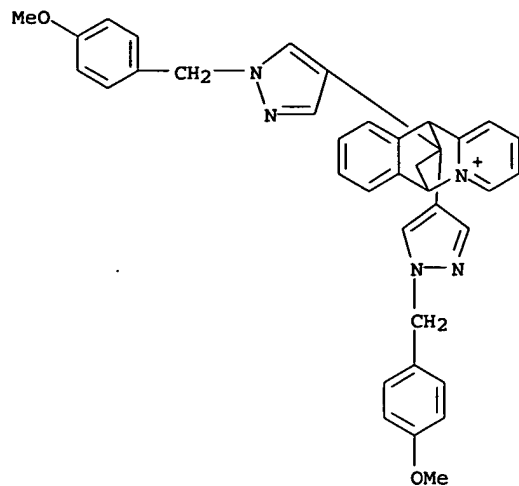
CN 6,11-Ethanobenzo[b]quinolizinium, 6,11-dihydro-12,12-bis[1-[(4-methoxyphenyl)methyl]-1H-pyrazol-4-yl]-, perchlorate (9CI) (CA INDEX NAME)

CM 1

CRN 170486-82-5

CMF C37 H34 N5 O2

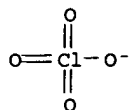
10/625024



CM 2

CRN 14797-73-0

CMF Cl O4



RN 170486-90-5 CAPLUS

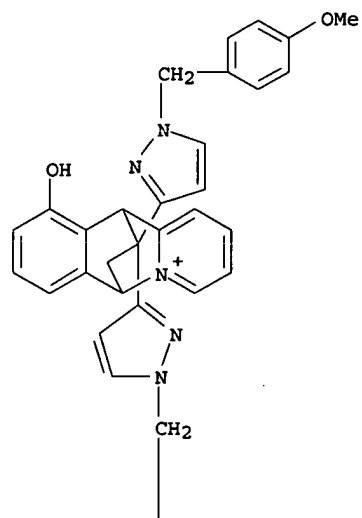
CN 6,11-Ethanobenzo[b]quinolizinium, 6,11-dihydro-10-hydroxy-12,12-bis[1-[(4-methoxyphenyl)methyl]-1H-pyrazol-3-yl]-, perchlorate (salt) (9CI) (CA INDEX NAME)

CM 1

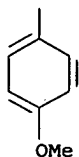
CRN 170486-89-2

CMF C37 H34 N5 O3

PAGE 1-A

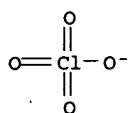


PAGE 2-A



CM 2

CRN 14797-73-0  
CMF C1 O4

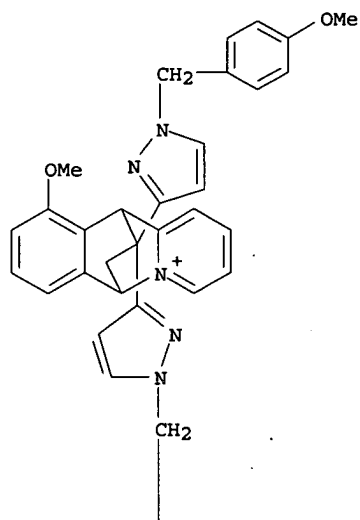


RN	170486-97-2	CAPLUS
CN	6,11-Ethanobenzo[b]quinolizinium, 6,11-dihydro-10-methoxy-12,12-bis[1-[(4-methoxyphenyl)methyl]-1H-pyrazol-3-yl]-, perchlorate (9CI) (CA INDEX NAME)	

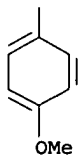
CM 1

CRN 170486-96-1  
CMF C38 H36 N5 O3

PAGE 1-A



PAGE 2-A

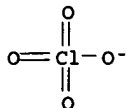


10/625024

CM 2

CRN 14797-73-0

CMF Cl O4



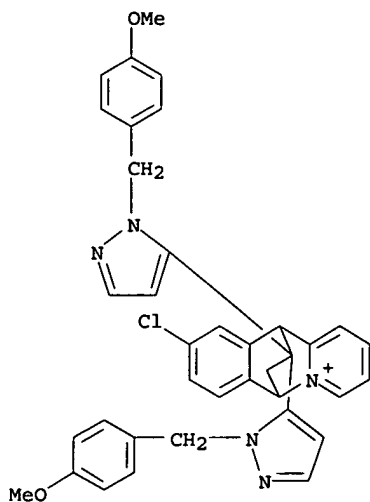
RN 170487-19-1 CAPLUS

CN 6,11-Ethanobenzo[b]quinolizinium, 9-chloro-6,11-dihydro-12,12-bis[1-[(4-methoxyphenyl)methyl]-1H-pyrazol-5-yl]-, perchlorate (9CI) (CA INDEX NAME)

CM 1

CRN 170487-18-0

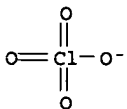
CMF C37 H33 Cl N5 O2



CM 2

CRN 14797-73-0

CMF Cl O4



RN 170487-29-3 CAPLUS

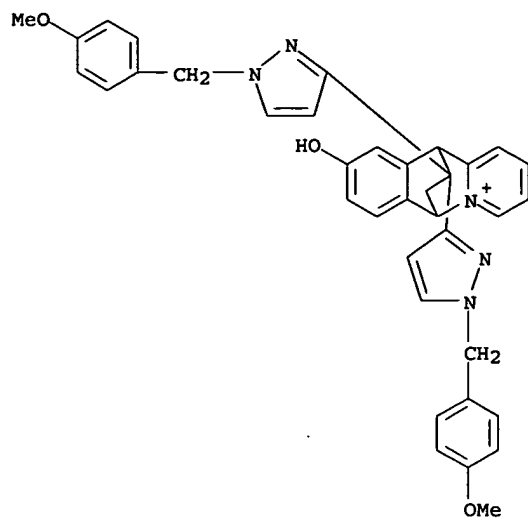
CN 6,11-Ethanobenzo[b]quinolizinium, 6,11-dihydro-9-hydroxy-12,12-bis[1-[(4-methoxyphenyl)methyl]-1H-pyrazol-3-yl]-, perchlorate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 170487-28-2

CMF C37 H34 N5 O3

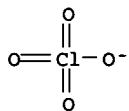
10/625024



CM 2

CRN 14797-73-0

CMF C1 O4



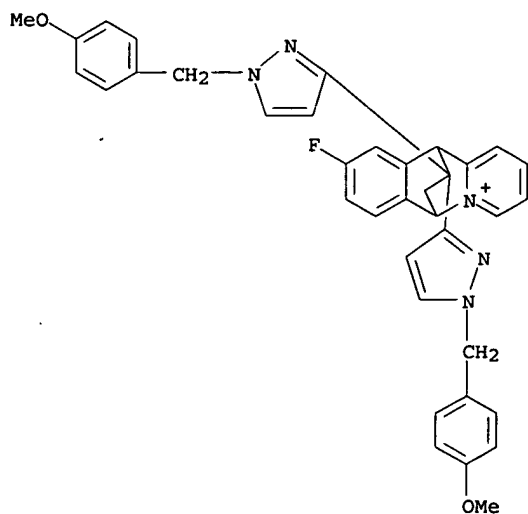
RN 170487-34-0 CAPLUS

CN 6,11-Ethanobenzo[b]quinolinizinium, 9-fluoro-6,11-dihydro-12,12-bis[1-[(4-methoxyphenyl)methyl]-1H-pyrazol-3-yl]-, perchlorate (9CI) (CA INDEX NAME)

CM 1

CRN 170487-33-9

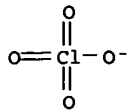
CMF C37 H33 F N5 O2



CM 2

CRN 14797-73-0

CMF Cl O4



L15 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1995:928116 CAPLUS

DN 123:339769

TI Preparation of 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA receptor antagonists

IN DeHaven-Hudkins, Diane L.; Dority, John A., Jr.; Earley, William G.; Kumar, Virendra; Mallamo, John P.; Miller, Matthew S.; Subramanyam, Chakrapani

PA Sterling Winthrop Inc., USA

SO Can. Pat. Appl., 220 pp.

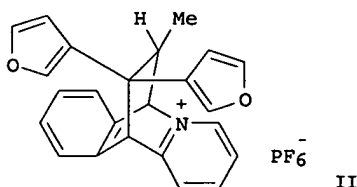
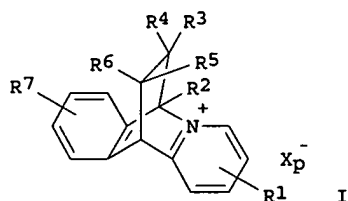
CODEN: CPXXEB

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 2131966	AA	19950315	CA 1994-2131966	19940913
	US 5554620	A	19960910	US 1994-283317	19940729
PRAI	US 1993-121127	A	19930914		
	US 1994-283317	A	19940729		
OS	MARPAT 123:339769				
GI					



AB Title compds. (I; R1, R7 = H, halo, alkyl, alkoxy, etc.; R2 = H, alkyl, cyano, alkoxycarbonyl; R3, R4 = H, alkyl; R3R4 = alkylidene, alkylene; R5, R6 = Ph, heteroaryl, heterocyclyl, etc.; R3R5, R4R6 = atoms to form a bicyclic ring system; X- = anion; p = 0 when R7 is neg. charged; p = 1 when R7 is not neg. charged) were prepared. Thus, 1,1-bis(3-furyl)propene was cyclocondensed with benzo[b]quinolizinium hexafluorophosphate (preparation each given) to give, as 1 of 2 regioisomers, title compound II which had IC50 of 11.4nM against NMDA-induce neurotoxicity in cultured neurons in vitro.

IT 170485-95-7P 170486-26-7P 170714-64-4P  
170714-68-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

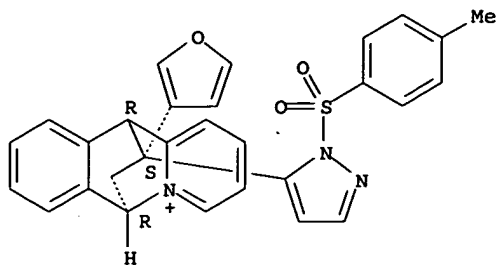
(preparation of 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA receptor antagonists)

RN 170485-95-7 CAPLUS

CN 6,11-Ethanobenzo[b]quinolizinium, 12-(3-furanyl)-6,11-dihydro-12-[1-[(4-methylphenyl)sulfonyl]-1H-pyrazol-5-yl]-, bromide,  
(6α,11α,12S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

10/625024

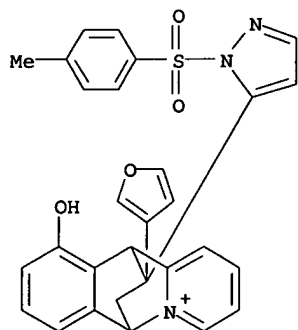


● Br<sup>-</sup>

RN 170486-26-7 CAPLUS  
CN 6,11-Ethanobenzo[b]quinolizinium, 12-(3-furanyl)-6,11-dihydro-10-hydroxy-12-[1-[(4-methylphenyl)sulfonyl]-1H-pyrazol-5-yl]-, (6α,11α,12S\*)-, perchlorate (salt) (9CI) (CA INDEX NAME)

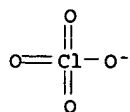
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CRN 170486-25-6  
CMF C29 H24 N3 O4 S



CM 2

CRN 14797-73-0  
CMF Cl O4

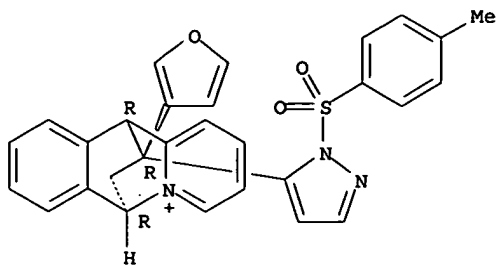


RN 170714-64-4 CAPLUS  
CN 6,11-Ethanobenzo[b]quinolizinium, 12-(3-furanyl)-6,11-dihydro-12-[1-[(4-methylphenyl)sulfonyl]-1H-pyrazol-5-yl]-, bromide, (6α,11α,12R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



10/625024



● Br<sup>-</sup>

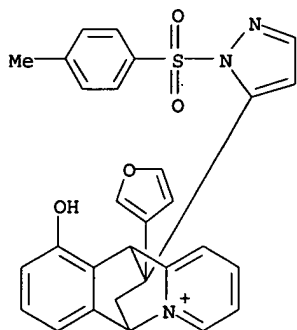
RN 170714-68-8 CAPLUS

CN 6,11-Ethanobenzo[b]quinolizinium, 12-(3-furanyl)-6,11-dihydro-10-hydroxy-12-[1-[(4-methylphenyl)sulfonyl]-1H-pyrazol-5-yl]-, (6 $\alpha$ ,11 $\alpha$ ,12R<sup>+</sup>)-, perchlorate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 170714-67-7

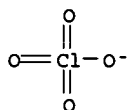
CMF C29 H24 N3 O4 S



CM 2

CRN 14797-73-0

CMF Cl O4



IT 170486-57-4P 170486-83-6P 170486-90-5P

170486-97-2P 170487-19-1P 170487-29-3P

170487-34-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA receptor antagonists)

RN 170486-57-4 CAPLUS

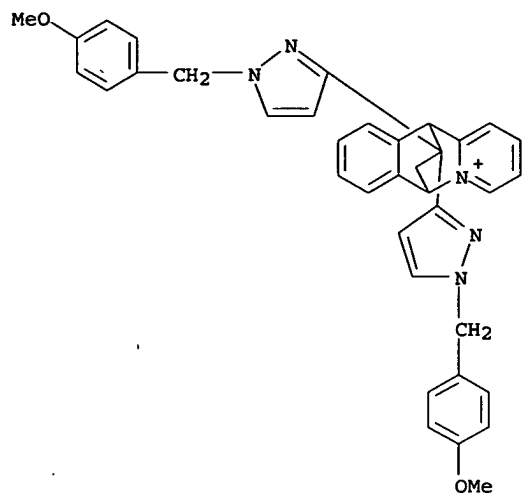
CN 6,11-Ethanobenzo[b]quinolizinium, 6,11-dihydro-12,12-bis[1-[(4-methoxyphenyl)methyl]-1H-pyrazol-3-yl]-, perchlorate (9CI) (CA INDEX NAME)

CM 1

CRN 170486-56-3

10/625024

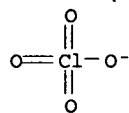
CMF C37 H34 N5 O2



CM 2

CRN 14797-73-0

CMF Cl O4



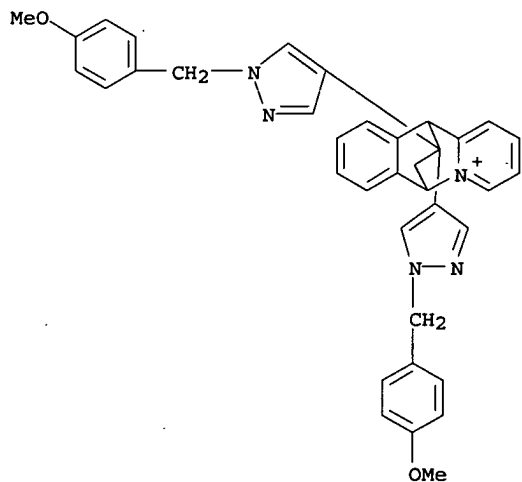
RN 170486-83-6 CAPLUS

CN 6,11-Ethanobenzo[b]quinolizinium, 6,11-dihydro-12,12-bis[1-[(4-methoxyphenyl)methyl]-1H-pyrazol-4-yl]-, perchlorate (9CI) (CA INDEX NAME)

CM 1

CRN 170486-82-5

CMF C37 H34 N5 O2

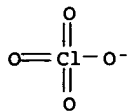


10/625024

CM 2

CRN 14797-73-0

CMF Cl O4



RN 170486-90-5 CAPLUS

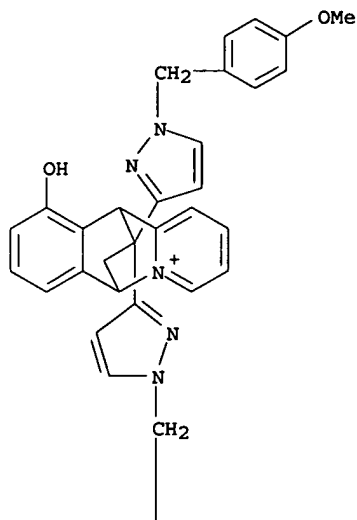
CN 6,11-Ethanobenzo[b]quinolizinium, 6,11-dihydro-10-hydroxy-12,12-bis[1-[(4-methoxyphenyl)methyl]-1H-pyrazol-3-yl]-, perchlorate (salt) (9CI) (CA INDEX NAME)

CM 1

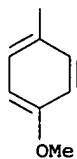
CRN 170486-89-2

CMF C37 H34 N5 O3

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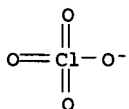
PAGE 2-A



CM 2

CRN 14797-73-0

CMF Cl O4



10/625024

RN 170486-97-2 CAPLUS

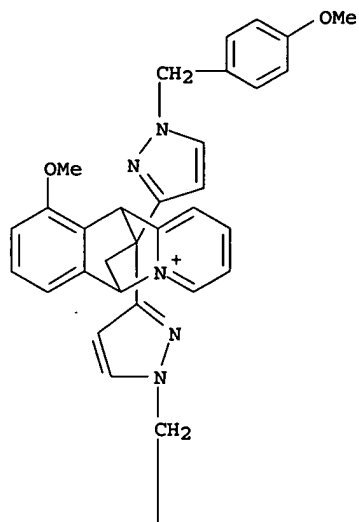
6,11-Ethanobenzo[b]quinolizinium, 6,11-dihydro-10-methoxy-12,12-bis[1-[(4-methoxyphenyl)methyl]-1H-pyrazol-3-yl]-, perchlorate (9CI) (CA INDEX NAME)

CM 1

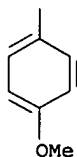
CRN 170486-96-1

CMF C38 H36 N5 O3

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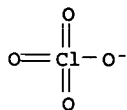
PAGE 2-A



CM 2

CRN 14797-73-0

CMF C1 O4



RN 170487-19-1 CAPLUS

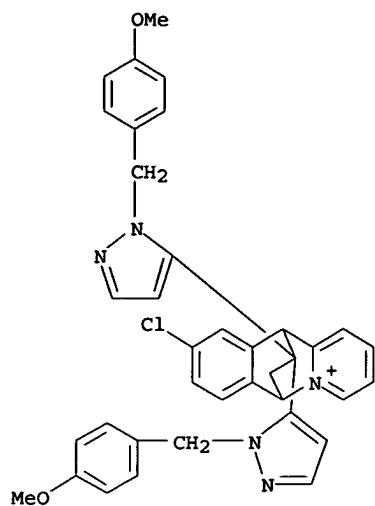
6,11-Ethanobenzo[b]quinolizinium, 9-chloro-6,11-dihydro-12,12-bis[1-(4-methoxyphenyl)methyl]-1H-pyrazol-5-yl]-, perchlorate (9CI) (CA INDEX NAME)

CM 1

CRN 170487-18-0

CMF C37 H33 C1 N5 O2

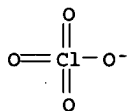
10/625024



CM 2

CRN 14797-73-0

CMF Cl O4



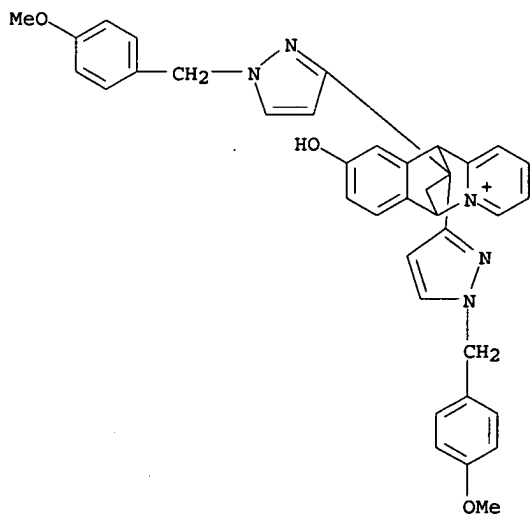
RN 170487-29-3 CAPLUS

CN 6,11-Ethanobenzo[b]quinolinizinium, 6,11-dihydro-9-hydroxy-12,12-bis[1-[(4-methoxyphenyl)methyl]-1H-pyrazol-3-yl]-, perchlorate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 170487-28-2

CMF C37 H34 N5 O3

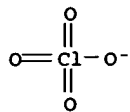


10/625024

CM 2

CRN 14797-73-0

CMF Cl O4



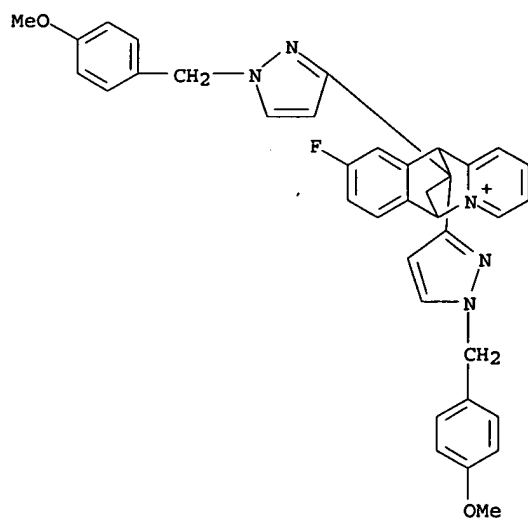
RN 170487-34-0 CAPLUS

CN 6,11-Ethanobenzo[b]quinolizinium, 9-fluoro-6,11-dihydro-12,12-bis[1-[(4-methoxyphenyl)methyl]-1H-pyrazol-3-yl]-, perchlorate (9CI) (CA INDEX NAME)

CM 1

CRN 170487-33-9

CMF C37 H33 F N5 O2



CM 2

CRN 14797-73-0

CMF Cl O4

